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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,109	12/02/2003	Peter Francis Joseph O'Hare	5759-67433-01	4401

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EXAMINER
ZARA, JANE J

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
07/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,109	O'HARE ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23* is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 3-27-07.

Claims 1-23 are pending in the instant application.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 1-3, 10, 17, 18, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Hare et al (WO 97/05265) for the reasons of record set forth in the Office action mailed 9-27-06.

Applicant's arguments filed 3-27-07 have been fully considered but they are not persuasive. Applicant argues that the instant rejection is not proper because O'Hare does not teach the specific types of stable aggregated particles and that they are an association of VP22 with an oligonucleotide or a polypeptide. Applicant also argues that the teachings of O'Hare do not disclose the specified methods used for making the aggregated particles.

Contrary to Applicant's assertions, O'Hare does teach aggregated compositions and methods of making aggregated compositions comprising a VP22 polypeptide or a fragment thereof having a transport function of VP22, which optionally comprise amino acid sequences 159-301 of SEQ ID NO: 12, encoding VP22, a protein, polypeptide,

nucleic acid polynucleotide or oligonucleotide to be transported via VP22, associated either covalently or non-covalently, and optionally encapsulated within a liposome for delivery into target cells in vitro and a pharmaceutically acceptable excipient, which aggregated composition has a particle size between 0.1 and 5 microns. O'Hare also teaches the mixing of the solution comprising the VP22 polypeptide and polypeptide or oligonucleotide which is delivered to cells in vitro. The steps recited in the claims are those disclosed by O'Hare. For these reasons, the instant rejection is maintained.

Claims 1-3, 15, 16, 18, 20, 21 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Hare et al (USPN 6,184,038) for the reasons of record set forth in the Office action mailed 9-27-06.

Applicant's arguments filed 3-27-07 have been fully considered but they are not persuasive. Applicant argues that the instant rejection is not proper because O'Hare does not teach the specific types of stable aggregated particles and that they are an association of VP22 with an oligonucleotide or a polypeptide. Applicant also argues that the teachings of O'Hare do not disclose the specified methods used for making the aggregated particles.

Contrary to Applicant's assertions, O-Hare does teach aggregated compositions and methods of making aggregated compositions comprising a VP22 polypeptide or a fragment thereof having a transport function of VP22 (and which optionally comprise amino acid sequences 159-301 of SEQ ID NO: 12), an oligonucleotide of at least 10 nucleobases, a pharmaceutically acceptable excipient, which aggregated composition

has a particle size between 0.1 and 5 microns, whereby a solution comprising the VP22 polypeptide and oligonucleotide is mixed in solution and is delivered to cells in vitro (See entire document, especially figures 5, 6 and 9; col. 8, line 15 - col. 10, line 38; col. 11, line 62 - col. 12, line 5; col. 12, lines 59-67; claims 1-8 of USPN 6,184,038).

Claims 1- 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hare as applied to claims 1-3, 10, 15-18, 20, in view of Hawley-Nelson et al and Schwartz et al, the combination further in view of Moyer et al for the reasons of record set forth in the Office action mailed 9-27-06.

Applicant's arguments filed 3-27-07 have been fully considered but they are not persuasive. Applicant argues that the instant rejection is not proper because O'Hare does not teach the specific types of stable aggregated particles and that they are an association of VP22 with an oligonucleotide or a polypeptide. Applicant also argues that the teachings of O'Hare do not disclose the specified methods used for making the aggregated particles.

Contrary to Applicant's assertions, O'Hare does teach aggregated compositions and methods of making aggregated compositions comprising a VP22 polypeptide or a fragment thereof having a transport function of VP22, which optionally comprise amino acid sequences 159-301 of SEQ ID NO: 12, encoding VP22, a protein, polypeptide, nucleic acid polynucleotide or oligonucleotide to be transported via VP22, associated either covalently or non-covalently, and optionally encapsulated within a liposome for delivery into target cells in vitro and a pharmaceutically acceptable excipient, which

aggregated composition has a particle size between 0.1 and 5 microns. O'Hare also teaches the mixing of the solution comprising the VP22 polypeptide and polypeptide or oligonucleotide which is delivered to cells in vitro. The steps recited in the claims are those disclosed by O'Hare. For these reasons, the instant rejection is maintained.

Applicant also argues that the instant rejection is not proper because Hawley Nelson describe entirely different peptide nucleic acid complexes and teaches transfection compositions and the Moyer citation fails to mention any aggregates, nor disclose the use of VP22. Applicant also agrues that Schwartz teaches cationic lipids, and the instant invention merely encapsulates already formed VP22 aggregates.

Applicant is arguing each of the references in isolation to rebut the instant obviousness rejection, but, contrary to Applicant's assertions, these combined teachings properly render the instant invention obvious. Contrary to Applicant's assertions, Hawley-Nelson teaches methods of forming aggregated compositions and their subsequent delivery to target cells in vitro comprising a VP22 polypeptide with transport function and a nucleic acid of at least 10 nucleobases (in a 1:1 ratio, and having a particle size between .1 to 5 microns), and a pharmaceutically acceptable excipient, and which VP22 polypeptide is optionally part of a fusion protein, and which aggregated compositions are made by mixing the solution comprising a VP22 polypeptide and a polynucleotide, and optionally further comprising mixing and encapsulating the polypeptide and nucleic acid within a liposome. Schwartz is properly relied upon to teach methods of making and using aggregations comprising liposomes, proteins, peptides, glycoproteins and polynucleotides, which polynucleotides include antisense or

ribozyme molecules which contain phosphorothioate internucleoside linkages, and which oligonucleotides may be circular, and which oligonucleotides contain a detectable label, and which aggregates are delivered to target cells. And Moyer teaches incorporation of cleavable linkages within various constructs which are destined for target cell, whereby cleavage occurs within the target cells by the appropriate enzymes, and the joined polypeptides or proteins are released.

Contrary to Applicant's assertions, it would have been obvious to one of ordinary skill in the art to make and use aggregated compositions comprising the binding domain of the VP22 polypeptide and further comprising a polynucleotide, and/or another peptide or protein, because such compositions had been taught previously by O'Hare et al for delivery to target cells. One of ordinary skill in the art would have been motivated to use such compositions for cellular delivery because such transduction domains as the binding domain of VP22 have been used for crossing target cell membranes, as taught previously by O'Hare et al, and therefore the inclusion of VP22 within such compositions was found to enhance the cellular uptake of the compositions, and furthermore also found to enhance localization of the complexes or aggregates within the nuclei of target cells.

Aggregates are an inherent property resulting from the mixing of VP22 polypeptide and oligonucleotides. (Aggregates will also form under CaP transfection conditions.) And, contrary to Applicant's assertions, one of ordinary skill in the art would have expected that aggregates form upon mixing of the amphipathic (cationic) liposomes with the (anionic) polynucleotides and proteins or polypeptides because such

aggregation is well known in the art and has been taught previously by many in the art, including Schwartz. It would also have been obvious to one of ordinary skill in the art to make and use aggregated compositions comprising liposomes, the transport domain of the VP22 polypeptide and further comprising a polynucleotide and another peptide or protein, because such compositions had been taught previously by O'Hare et al for delivery to target cells. For these reasons, the instant rejection is maintained.

Allowable Subject Matter

Claim 23 appears free of the prior art searched.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
6-22-07